PHARMACEUTICAL COCRYSTALS OF BIGUANIDE DRUGS: METFORMIN CASE STUDY

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ABSTRACT

US FD's released draft guidelines for regulatory classification of pharmaceutical cocrystals (PCC) of active pharmaceutical ingredients (APIs) enforced by the increased interest for research on multicomponent crystal with pharmaceutical relevance brought an attention to scientiffic community broadly to spread the deffinition of PCC as solids that are crystalline single phase materials composed of two or more different molecular and/or ionic compounds generally in a stoichiometric ratio [1,2].
Well know antidiabetic drug metformin (MET) was chosen as drug model (DM) with basic property for cocrystallization with range of coformers (CF) from the classes of carboxylic and inorganic acids in order to prepare PCC.
Following twelve PCC with metfomin were obtained: MET/ Acetic Acid1/1 (molar ratio) *M/M*; MET/ Maleic Acid 1/1 *M/M*; MET/Fumaric Acid 1/0.5 *M/M*; MET/Oxalic Acid Hydrate 1/1/1/ *M/M/M*; MET/Malonic Acid 1/1 *M/M*; MET/Succinic Acid 1/0.5 *M/M*; MET/Salicylic Acid 1/1 *M/M*; (7) MET/Picric Acid 1/1 *M/M*, (8) MET / Picric Acid 1/2 *M/M* and MET/Saccharine 1/1 *M/M* (obtained two polymorphic forms); MET/Phosphoric Acid/Dihydrate 2/1/2 *M/M/M* and MET/Nitric Acid 1/1 *M/M*.
All these PCCs form a complex network of H-bonds and other intermolecular interactions. The systematic analysis of the molecular geometries and crystal packing indicate correlations between the intermolecular H-bonds with the ΔpKa values in the PCCs obtained.

REFERENCES

[1] Guidance for Industry "Regulatory Classification of Pharmaceutical Co-Crystal http//www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm
[2] Aitipamula, S., *et al.*, Polymorphs, Salts, and Cocrystals: What's in a Name?, Cryst. Growth Des. 2012, 12, 2147−2152